TO COMPARE THE SENSITIVITY OF URINARY POLYMERASE CHAIN REACTION WITH INTRAVENOUS UROGRAPHY AND URINE ACID FAST BACILLI IN A CLINICALLY SUSPECTED CASE OF GENITO URINARY TUBERCULOSIS

Dissertation submitted in partial fulfillment of the requirements of

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CERTIFICATE

This is to certify that this dissertation entitled **"TO COMPARE THE SENSITIVITY OF URINARY POLYMERASE CHAIN REACTION WITH INTRAVENOUS UROGRAPHY AND URINE ACID FAST BACILLI IN A CLINICALLY SUSPECTED CASE OF GUTB"** submitted by **Dr. S.SUDHAKARAN** appearing for **M.Ch (Urology)** degree examination in August 2014 is a original bonafide record of work done by him under direct supervision and guidance in partial fulfillment of requirement of the Tamil Nadu Dr.M.G.R. Medical University, Chennai during Academic year 2011-2014.

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TABLE OF CONTENTS

ABBREVIATIONS

AFB	Acid Fast Bacilli
ADPKD	Autosomal Dominant Poly cystic kidneys
AIDS	Acquired Immuno Deficiency Syndrome
ATT	Anti Tuberculosis Treatment
BCG	Bacilli Calmette Guerin
CMI	Cell Mediated Immunity
CT	Computerised Tomogram
DNA	Deoxyribo Nucleic Acid
ESRD	End Stage renal Disease
GUTB	Genito Urinary Tuberculosis
HIV	Human Immuno deficiency Virus
IVU	Intra Venous urogram

LUTS	Lower Urinary Tract symptoms
MTB	Mycobacterium Tuberculosis
PCR	Polymerase Chain Reaction
PT	Pulmonary Tuberculosis
RGP	Retrograde pyelogram
USG	Ultra Sonogram
SCC	Squamous Cell Carcinoma
WHO	World Health Organisation

INTRODUCTION

INTRODUCTION

Tuberculosis is as old as human race. Old literature shows evidence of Mycobacterium Tuberculosis even in egyptian mummies. During the 19th century this disease was called as consumption disease as it was considered a major killer. With the introduction of anti tuberculous drugs, there is decrease in incidence of new cases as well as death due to tuberculous infection, but still tuberculosis is a large public health problem.

In healthy persons, tuberculous infection is clinically in apparent. 10% to 15% of people who are infected with TB are prone to develop GUTB.

Poor nutrition, people living in crowded situations and poverty are the greatest risk factor for acquiring this disease. The recent trend of resistant strains of M.Tuberculosis form a major obstacle for the treating physician.

The recent resurgence of tuberculosis and its association with HIV infection leading onto acquired Immuno Deficiency Syndrome (AIDS) in another worrying problem.

GUTB because of its varying radiological appearance and non specific clinical presentation poses a significant health problem. About 30% of extra - pulmonary TB involves the urogenital tract, roughly about 5% of all cases of tuberculosis.

GUTB is a disease of male pre-dominance, the most common age group affected is of sexually active period 20 to 40 years.

GUTB usually manifest about 15-20 years after initial pulmonary infection. Tuberculosis is most common opportunistic infection in HIV patients.70% of AIDS patients have extra pulmonary lesions also.

The various investigations play a very significant role in the diagnosis, planning treatment, following up of patients after treatment as GUTB has a non specific clinical presentation.

AIM

AIM

'To compare the sensitivity of Urinary Polymerase chain reaction(PCR) with intravenous urography and urine acid fast bacilli culture in a clinically suspected case of GUTB'

MATERIALS & METHOD

MATERIALS AND METHODS

1. **Study Group** : patients who are admitted in Kilpauk Medical College and Govt. Royapettah hospital with irritative lower urinary tract symptoms due to GUTB

2. **Study Design** : prospective clinical study

3. **Study Period** : 1 Year from 1/2013 to 12/2013

4. **Inclusion Criteria** :

   Patients with complaints of

   1) irritative voiding symptoms

   2) sterile pyuria

   3) hematuria

   4) constitutional symptoms – low grade fever

      – loss of appetite/weight

   5) flank pain

   6) scrotal sinus / swelling

EXCLUSION CRITERIA :

OTHER CAUSES OF STERILE PYURIA,

IRRITATIVE LOWER URINARY TRACT SYMPTOMS,

HEMATURIA ARE RULED OUT .

REVIEW OF LITERATURE

REVIEW OF LITERATURE

Tuberculosis is one of the leading cause for infection related morbidity and mortality. Extra-pulmonary TB accounts for 20-25% of which genito urinary TB forms <5%, Timely diagnosis and treatment can prevent sequelae of this disease.

Clinical Presentation GUTB :

GUTB has a wide and varied presentation. Some of the presenting complaints of the patients include

Irritative voiding symptoms

1) Urgency
2) Dysuria
3) Increased frequency
4) Rarely urge incontinance
5) Nocturia

Hematuria – 10% macroscopic hematuria

50% microscopic hematuria

Flank Pain – dullaching, dragging type of pain

- Due to hydronephrosis, stretching of renal capsule

constitutional symptoms

chronic low grade fever, night sweats

loss of weight, loss of appetite

malaise, lassitude

Rec. UTI

Recurrent or resistant UTI, negative culture for any normal bacterial infection

Scrotal mass

Painless hydrocele – secondary, epididymal thickening, tender cord structures

Fistulae

May be seen in renal TB with communication to the

1) GIT
2) Skin
3) Retro peritoneum

Fistula can also be seen in relation to testis and epididymis. Usually the sinus opening is seen in the posterior aspect of scrotum which is of chronic duration with discharge and undermined edges.

Infertility

Mostly seen in females with features of tubal block, involvement of ovaries, endometrium.

In males apart from kidney prostate and seminal vesicle are one of the primary organs to be involved in GUTB.

Renal failure

Renal failure is a late feature of GUTB. Although GUTB is bilateral disease it is usually involves only one kidney at a time. Hence very rarely patients go in for this complication.

All patients were subjected to following routine investigations :

1) urine routine examination
2) urine culture and sensitivity
3) complete heamogram
4) renal function test
5) USG

In addition the following specific investigation were done.

1) **Urine - Acid Fast Bacilli**

2) Urinary PCR for Acid Fast Bacilli

3) Intra Venous Urogram

Urine for AFB:

Either multiple early morning samples(2to3) or consecutive 24 hours urine samples were collected for AFB analysis. The collected urine is mixed well and 50ml of urine is taken is a Test tube, centrifuged at 3000 Rpm for 30mins. The supernatent fluid is discarded, The sediment is placed on a slide and zeel-neelson staining procedure is followed.

This slide is heated for 3 t 5 minutes with carbol fuchsion till boiling.
Slide is washed with water and decolorised with 20% sulphuric acid and followed by 95% ethanol.

The slide is counter stained with methylene Blue and observed under microscope by oil immersion technique , the myco bacteria appears as bright red or pink rods against a Blue or green background.

The positively rate of urine AFB is 41% - single sample

for multiple samples, it ranges from 40 to 60%.

II. Intra venous urogram:

Details are in the subsequent part of literature.

After confirming the renal function test to be normal, patient was planned for IVU.

Pre-procedure preparation

1) overnight starvation

2) T. Bisacodyl 002

activated charcoal -2-2.2

3) informed, written consent.

4) good hydration of patient

In the radiology department, dose of low osmolar, non-Ionic contrast media at the rate of 1mg/1kg body weight is calculated and given as IV Bolus. Serial pictures are taken at 3,5,15,45 minutes and post-void pictures. In certain circumstances, 6 hrs delayed pictures are also taken and interpreted, if needed prone pictures are also taken.

The findings in IVU include.

1) kidneys – dilated calyx, infundibular stenosis, hydronephrosis

Non functioning kidney

2) Ureter – single ureteric stricture , multiple stricture

3) Bladder -Small capacity bladder

Thimble bladder

The earliest changes in GUTB are

1. Loss of sharpness of minor calyx, blunting of calyx.

2. Moth eaten appearance of calyx -erosion of calyx

3. Infundibular stenosis

4. Phantom calyx

5. Renal cavitation

6. Pseudo tumor, Pseudo calculi

7. Renal scar

8. Non functioning kidney

III. Urine – PCR for AFB

Entire first morning sample of urine is collected. The urine is centrifuged 3000rpm for 30 minutes, the resultant is divided into 3 portions in 20mm tris. DNA extraction is done by sterile laminar flow. DNA is added to reaction mixture. Post amplification identification was done for MPB-64 gene of MTB complex. DNA was extracted with proteinase – K (1mg/ml) and 0.5% tween 20 followed with phenol or chloroform which is again precipitated with ethanol. The sequence of primer and probe are as follows:

Primer – I – 460-475-5TCC-TTCC-3^1

Primer – II – 700-681-5GTC-GCCA-3^1

Probe – 601-617-5CTT-AGT-3^1

Amplification reaction :

It is done with 50 micro liters of reaction mixture – 10mm tris hcl, 50mm nacl, 1.5mm mgcl2, gelatine – 0.01%, 0.4 micro liters of primer 1,2,1.25 units of taq polymerise, 10 micro liters of extracted dna run at 94^oC for 2 minuts.

Annealing

It is done at 58 to 60 ^oC for 2 minutes

Extension

This is the last stage of this test done at 72 ^{o}C for 2 minutes, 40 cycles with negative and positive controls the amplified product analysis done on 2% agar with ethironbromide.

Confirmation :

Result confirmation is done with southern blot and hybridization technique. If 241Bp is positive on agar gel the urinary PCR reaction is considered positive. If absent test is considered negative.

The sensitivity of urinary PCR – 97%

The specificity of urinary PCR – 76%.

Urinary PCR is very much useful in paucibacillary conditions. It gives a faster and specific result. It can detect 1 bacteria to about 10 organisms. Urinary PCR is specific for MTB complex – M tuberculosis, M bovis

False negativity can range form 5%. There is no cross reaction false negativity is due to

1) Presence of inhibitors
2) Unequal distribution of bacteria

False positivity is due to presence of amplicons, dead bacteria.

PATHALOGY:

Tuberculosis is an important public health problem the WHO estimates new TB cases accounts for about 34% in South eastern Asia region when comparing globally.

Timely diagnosis and treatment will prevent complications GUTB is the second most form of extra pulmonary tuberculosis. Kidney is the primary organ involved in urology it has a varied presentation most commonly as irritative voiding symptoms. The frequency of organ involvement is kidney, bladder, tubes and scrotem

GUTB arises from spread of PT through blood stream. Active GUTB may manifest 5 to 20 years after PT. 8 to 15% of patients with PT are prone for GUTB.

The various ways of presentation include

1) Irritative voiding symptoms
2) Flank pain with pyelonephritis
3) Incidental diagnosis in known case PT
4) Renal hydronephrosis

5) Hemospermia
6) Recurrent or resistant UTI
7) Renal failure
8) Non-healing wound, sinus, fistula

Other symptoms include fever, weight loss, anorexia, backache, abdominal pain

Causative organism

MTB, a gram positive rod and obligate pathogen is the most common cause of GUTB followed by M bovis.

Spread of Tuberculosis

Hematogenous spread of MTB from a primary foci in lungs, bone and other organs. BCG following intra vesical instillation can cause renal lesion via reflex in 0.1% of patients.

Spread of infection

During primary infections alveolar macrophages engulf one or more mycobacteria. Due to high resistance to destruction mycobacteria multiply within macrophages ad result in hematogenous and lymphatic spread with

seeding of MTB all over the body.

The primary organs of GUTB involved are kidney, prostate and seminal vesicles. Other organs include bladder, epididymis. In some patients acquired CMI develops which inhibits MTB multiplication leading to microscopic granuloma. Healing may occur at this stage. In immuno competant patients these granuloma may heal or remain stable. It measures about 3mm in diameter hence could not be visualised by any investigation.

Reactivation of Tuberculosis

If there is host immune deficiency, reactivation or reinfection occurs it is proved that reduced level of 25-OH-vitamin D level causes CMI deficiency which can lead to reactivation of tuberculosis. One or more tubercles joined to form macroscopic granuloma. The latent period may vary from 5 to 20 years. The morphology of the lesion is based on

1) Site of infection
2) Virulence of organism
3) The immune status of the patient
4) In immune competant patients lesios are usually well formed granuloma with central caseation.

These lesions can occur in different areas of same kidney

In the kidneys the bacteria is lodged in the periglomerular capilliaries and form microscopic granuloma usually bilaterally. Severe infection is mostly unilateral

Parenchymal changes

Initially medulla of the renal parenchyma is spared. The upper and lower poles of the kidney are the most common site. The cortical granuloma enlarged and join leading to bacillary spilling down the nephron.

These bacteria are trapped in the narrow segment of loop of henle. This act as a new foci of infection within the renal pyramid. This papillary lesions cavitate, caseate and forms ulcero – cavernous lesions and erode in to pelvi-calyceal system.

Papillary necrosis leads to formation of cavities and destroys adjacent parenchyma it may also involve collecting system by rupture of parts of papilla.

Massive destruction with granuloma formation may appear as a mass lesion. These granuloma join to form large cavities. Secondary to abnormal cortisol production leads to hypercalcemia. Usually calcification is a feature of end stage of GUTB. But some times occurs in early stages. Sometimes UTB may

manifest as well circumscribed mutli septated cystic renal mass. In immuno suppressed individuals granuloma formation and caseation are not frequent. Pelvi calyceal system changes.

When bacteria are shed in the urine the disease involves urothelium of the renal pelvis, bladder,ureter at times the adjacent genital tract. Infection of the calyces, pelvis and ureter leads to mucosal thickening. Single or multiple calyces may be invloved. They may be unilateral or bilateral. Microscopic granuloma can further lead to ulceration in advance GUTB loss of renal parenchyma by caseation , formation of intra renal scars and strictures lead to obstruction of PCS. The most common site for stricture formation is at the normal narrowing such as calcyeal neck, pelvi-ureteric junction, uretero-vesical junction. Early scarring is reversible in most of the cases.

Appropriate steriod treatment are usually sufficient for managing early strictures along with ATT. Obstruction due to strictures and parenchymal caseation will destroy the entire kidney. Paranchymal destruction is depended upon severity of obstruction. Either parenchymal caseation, necrosis, or calcification may dominate in the destruction of kidney. If obstruction predominates there may be hydronephrosis or hydrocalicosis. Hence GUTB

of the kidney is a competitive process between the destructive effects of the bacilli, obstruction of the urinary tract and the host defence mechanism and the healing mechanism which leads to

1) granulomas,
2) calcifications,
3) fibrosis,
4) stricture formation.

All these process lead to a non functioning, calcified kidney which is known as autonephrectomy. Since this autonephrectomised kidney may contain live bacteria these patients are adviced undergo nephretomy.

Tuberculous interstitial nephritis(TIN)

TB of the kidney may also occur insidiously this condition is called as TIN. If untreated may lead to renal failure. These bacilli if open into the interstium may lead to isolated interstitial disease. These patients will not have sterile pyuria, hematuria, demonstration of AFB in urine which leads to a diagnostic problem. Histology from the lesions will show chronic TIN which may or may not be associated with granuloma or caseation with proper staining AFB can be demonstrated on histology. These patients may have reduced

glomerular filtration rate if diagnosed early this can be over come by giving ATT and steriods. There are also reports that TIN can occur as a complication of intra vesical administration of BCG.

Renal failure

Incidence of renal failure in GUTB varies between 20-24% the various mechanism by which it occurs are

1) Following obstruction o f the urinary tract due to multiple strictures

2) Patients, may also have dystrophic calcification, renal amyloidosis,

3) Renal parenchymal infection causing obliterative end arteritis these

TIN is insidious in onset and may destroy the renal parenchyma. This is a form of renal TB which is culture negative. The kidneys on USG may show echogenic kidneys this disease is confirmed by AFB staining of the tissues.

There are reports which show GUTB is associated with glomerulonephritis most commonly focal proliferative glomerulo nephritis where immune deposits are seen sub epithelially.

GUTB are occasionally complicated by presence of adenocarcinoma but also transitional cell carcinoma been reported. Both these conditions underline the fact that renal tumors would have reactivated dormant TB foci. There are also reports which show the incidence of leukemia in GUTB. GUTB has also been

reported to occur in native ADPKD, in immune compromised transplant patients, renal replacement lipomatosis and in horseshoe kidneys.

COMPLICATIONS

Extra renal spread

GUTB may spread to perinephric and paranephric, retro peritonial areas there may be formation of fistulas involving the gastro intestinal tract, skin, lymph vessels, pleura, bronchus of the thoracic cavity. There are also reports of liver abscess occuring with GUTB.

Amyloidosis

It is a complication of chronic TB, these leads on to end stage renal disease in patients who are not treated early.

Squamous metaplasia

This process is a risk factor for the development of squamous cell carsinoma which is a complication infection of the renal pelvis and chronic inflamation.

Imaging studies

The findings in imaging are based upon the extent of disease there is a good correlation between the time of diagnosis, manifestation of disease and

severity of GUTB. Any delay in diagnosis will lead to end stage renal disease and renal failure.

Intravenous urography

GUTB mostly spreads through hematogenous route only 10-12 cases will show positive chest X-ray for TB. Extra pulmonary disease process including calcification of lymph nodes, prostate, vas deferens, adrenal gland, psoas abscess. There may be associated calcified granulomas in the liver spleen . there may also be associated spinal deformatis. Calcification in GUTB in plain xray is about 20-40% which may be one of the first sign in many cases. These calcifications may fine in character, best visualised in plain CT. Initially to start with the calcification are fine, faint and punctate which may join together. These calcification may also be amorphous, curvilinear and granular.

Focal globular calcification is feature of renal papillary necrosis. They may also appear as triangular ring like calcifications. Calcified caseous tissue appearing less dense, homogenous resembling ground glass is called as **putty kidney**. It is called putty like kidney if the calcification is more than 1 cm.

The pathogmonic feature of renal TB is lobar calcification with peripheral rim of calcification. This is a feature of advance renal TB. This condition may be associated with **Autonephrectomy**. This shows that the renal destruction GUTB involves lobe by lobe. The presence of hydrocalicosis pushes the normal renal parenchyma to the periphery. This causes the calcification to appear as lobar rims.

Gow etal proposed that calcification in renal TB is a poor prognostic sign, if not intervened early it may lead to ESRD, renal failure. About 15-20% incidence of renal and ureteric calculi has been reported.

There are also reports of secondary non tuberculous infection which may also cause calcification or calculi in GUTB. Dense calcification which resemble calculi in the renal parenchyma called as **pseudo-calculi** have been reported. **Keratinizing SCC** have been reported in patients with chronic infection and inflammation in the kidney.

These calcification may also involve the ureter. The occurence of calcification of upper ureter along with renal calcification is a good evidence of renal TB. There may also be soft tissue calcification during the process of

healing associated with renal TB, these calcification are shapeless and called as **scarred calculi** they do not form the shape of renal pelvis.

Due to pelvis scarring the shape of pelvis is lost hence the calculi is of irregular shape. Upward pointing pelvic calculi may suggest **hiked up pelvis**. IVU gives both anatomical and functional details of the kidney. In about 10-15% of patients IVU may be normal in patients with GUTB. The earliest changes of GUTB in IVU are seen in the minor calyces which may appear as minimal calyceal dilation and there may be loss of sharpness of calyces due to mucosal edema.

As the disease advances the calyx may appear irregular, ragged, fuzzy and moth-eaten appearance. There are reports that papillary necrosis may be the first sign due to erosion of the papilla in TB, there may be caseating tuberculoma in the renal parenchyma which ruptures into calyx.

There are two types of papillary necrosis

1) central type

2) forniceal type

TB papillary necrosis may result from direct tissue destruction which is

feature of foniceal type. The central type of papillary necrosis may be due to ischemia and TB endarterities. There may be communication through the medullary cavity into the collecting system also irregular pools of contrast within the calyces.

In **advanced GUTB** there may be

1) Scar,
2) Fistula formation,
3) Cavities,
4) Strictures,
5) Mass lesions,
6) Perinephric abscess,
7) Autonephrectomy.
8) Calcification,

Cavitation

Due to the fibrotic deformity of the calyx the tips of the minor calyx are clubbed. As a result the minor calyx is filled with necrotic material.

The cavities can be of two types

1) obstructive type

2) non obstructive type.

In obstructive type, contrast material does not enter the cavity due to stenosis seen in RGP. Whereas in non obstructive type opacification of the calyx is seen only in RGP. The obstructive type should be monitored with serial USG.

The enlarging tuberculoma leads to parenchymal cavities. Those kidneys with cavitations are called as **ulcero-cavernous kidney**. These do not excrete contrast material, theses cavities open into the collecting system leading to TB bacilluria thereby the disease spreads to other parts of the urothelium.

Stricture / Scar :

The renal damage due to stricture is far more greater than renal tuberculoma . the three most common areas of fibrosis in GUTB are

1) lower ureter

2) PUJ

3) infundibulam

Fibrosis usually results from healing, stricture may also affect

1) calyceal neck

2) infundibulum

3) renal pelvis

The stricture may vary in number. How ever the renal pelvis is contracted and small. Due to traction from a strictured infundibulum there may be kinking of the renal pelvis due to parenchymal fibrosis. This type of kinking is called as **kerr's kink**.

Another entity called as **hiked up pelvis** due to stricture of the inferior margin of renal pelvis leading to cephalic retraction called as hiked up pelvis. Strictures leads to obstruction and dilation of the PCS which finally leads to pressure atrophy of the kidney.

This type of hydronephrosis may have irregular margin, irregular filling defect. Failure of visualisation of a calyx due to complete stenosis of infundibulum where by the contrast material does not enter the calyx is called as **phantom calyx.**

Another variant called as **amputated calyx** where only a samll infundibulum is seen, is another evidence of renal TB. Presence of parenchymal scars can be seen in about 40-50%.

Mass lesion :

In late stages of GUTB the disease may present as either hydronephrosis or TB granuloma.

Calcification

The characteristic pattern is lobar calcification.

There may also be pseudo calculai formation. In IVU the ureter may show

1) multiple stricture

2) single stricture with other findings

3) autonephrectomy

Autonephrectomy

In the advance stage GUTB, granulomatous destruction of renal parenchyma progress to autonephrectomy along with obstructive uropathy.

There are towo types of autonephrectomy

1) caseo-cavernous autonephretomy

2) shrunken, fibrotic autonephrectomy

Both types of autonephrectomy are non functional

Non functioning kidneys in GUTB may be due to

1) autonephrectomy
2) obstruction – ureteric obstruction, fibrosis
3) reno vascular hypertension – renal arterystenosis

The various other complication of renal TB are

1) fistulae
2) malignancy
3) peri nephricabscess
4) perinephritis
5) renal failure
6) psoas abscess

Bladder and urethral tuberculosis

The incidence of bladder TB in GUTB is about one third, the lesion starts as mucosal tubercle which joins to form multiple superficial ulcers. The features of this ulcer is

1) shallow ulcer

2) irregular

3) undermined edges

Patient may also present with ureteral obstruction if there is edema of the trigone mucosa.

IVU in bladder TB shows the following features:

1) small capacity bladder

2) irregular adhesive band

3) ulcers – filling defects

4) diffuse wall thickening

5) solid mass like lesion

The infection in bladder also involves muscular layer which leads to mural fibrosis as a result the bladder is contracted and thickened. The trigone may be fibrosed which produces a gaping ureteric orifice which leads to VU reflux.

The calcification in bladder may be a

1) nodular calcification

2) irregular rim like faint calcification

Uretheral Tuberculosis

Tuberculosis of male urethera is uncommon. It is usually due to secondary infection of prostate or kidney.

Patient may present with non specific stricture the most common site being bulbo membranous urethera.

There is a difficulty in confirming whether the stricture is due to

1) any instrumentation done to diagnose any pathology
2) specific TB infection

Patients may also present with

1) peri urethral abscess
2) multiple fistula of the urethra
3) water can perineum.

In women urethral tuberculosis is very uncommon.

Prostatic and Genital Tuberculosis.

The incidence of male Genital TB is about 30-90% in GUTB. It is most commonly seen in age group of 20-40 years, sexually active period. The various presentation of male genital TB includes

1) pain over testicles

2) painless enlargement of scrotum

3) sinus opening in the posterior scrotum

4) enlarged epididymis

the various other sites that may be involved are

1) vas deferens

2) prostate

3) seminal vesicle

4) rarely penis may be involved

The route of epididymis involvement are

1) lymphatic spread

2) hematogenous

3) retrograde spread from Vas

4) descending infection from kidney

rarely testis may involved without epididymal lesion.

The lesion starts from the globus minor because of good vascularity. Tuberculosis of the prostate may be due to

1) via infected urine
2) hematogenous
3) reactivation of initial infection.

The prostate may appear calcified and contracted. Vas deferens may be beaded, craggy. The seminal vesicles may appear fibrosed and contracted.

In women most common presentation of genital TB is infertility. The various route of infection are

1) direct extension from intestinal source
2) hematogenous
3) lymphatic spread
4) peritoneal implants

The fallopian tubes are the most commonly involved. They may present as

1) calcification
2) multiple strictures
3) pyosalpinx
4) hydrosalpinx

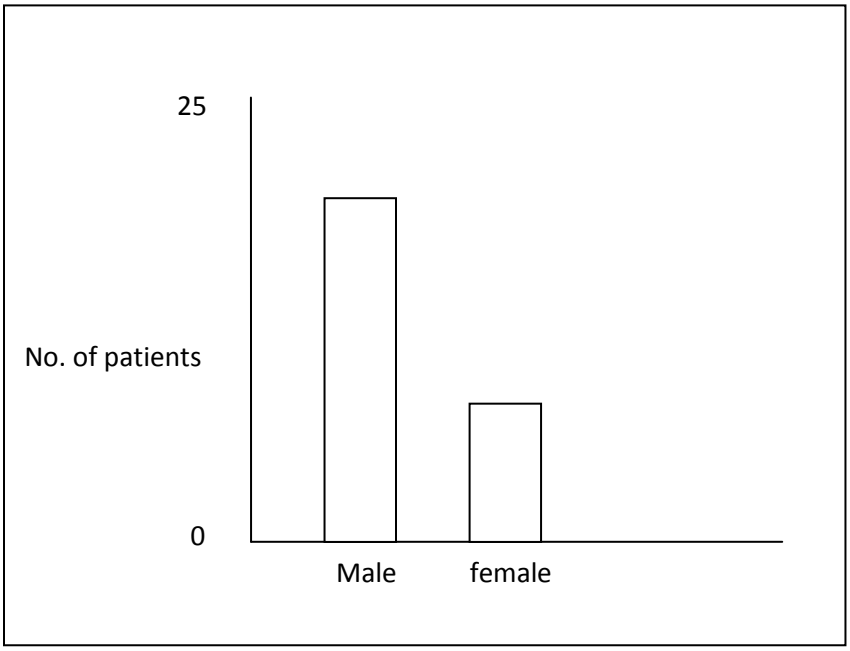
Rupture of a tuberculous infection may lead to tubo intestinal fistula.

Uterine endometrium is involved in 50%. The cavity may appear shrunken due to adhesion. The cervical canal is scarred.

The ovaries may involved and may present as tubo-ovarian mass.

ANALYSIS OF STUDY

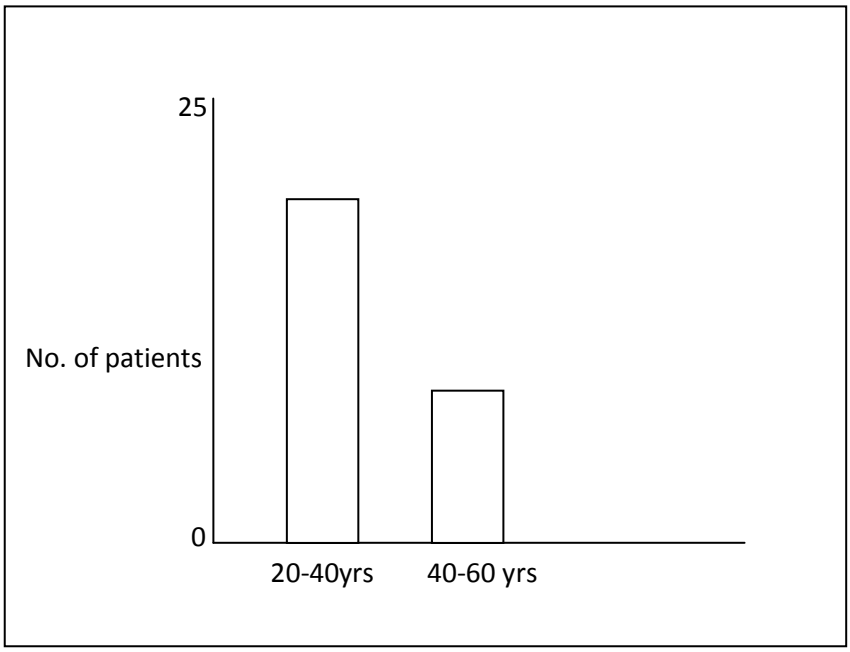
1) SEX DISTRIBUTION



MALE	18/25	76%
FEMALE	7/25	24%

76% of patients in the study group were males, remaining were females.

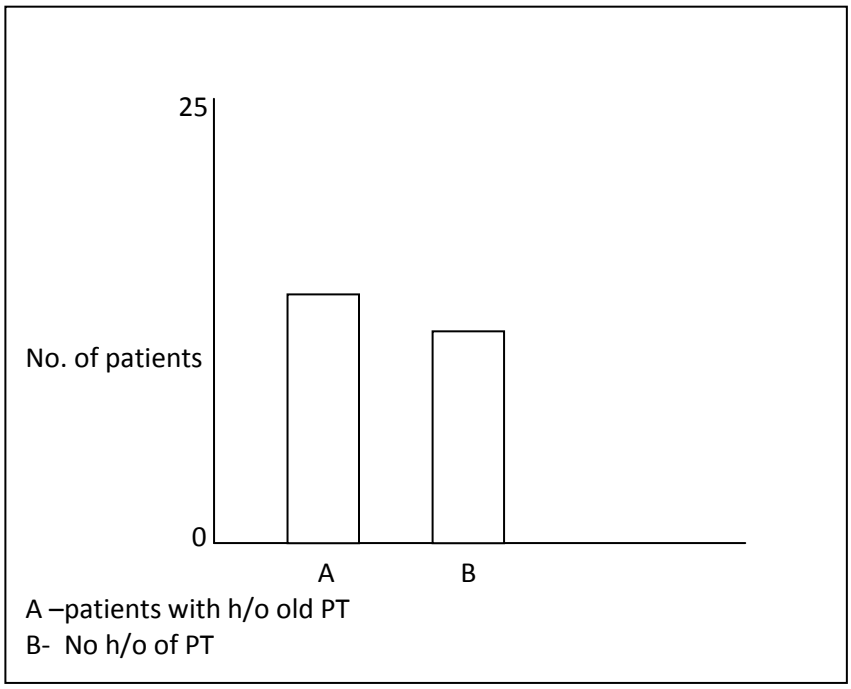
2. AGE DISTIRBUTION



20-40 yrs	20/25	80%
40-60 yrs	5/25	20%

80% of patients in our study were in the sexually active age group of 20 to 40 yrs.

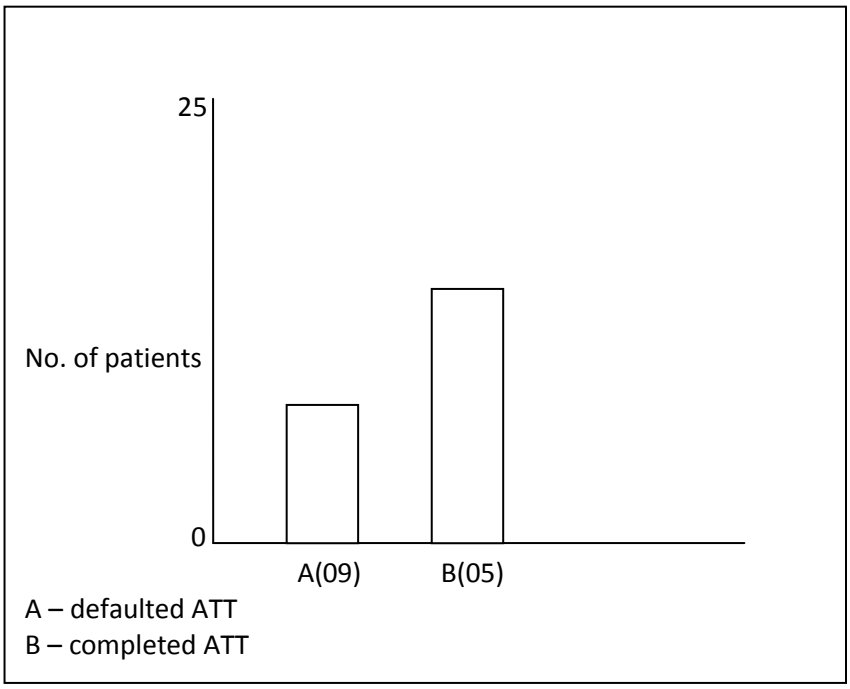
3)H/O, CONTACT WITH PT



A	14/25	56%
B	11/25	44%

56% of patients in our study group had past history of pulmonary tuberculosis

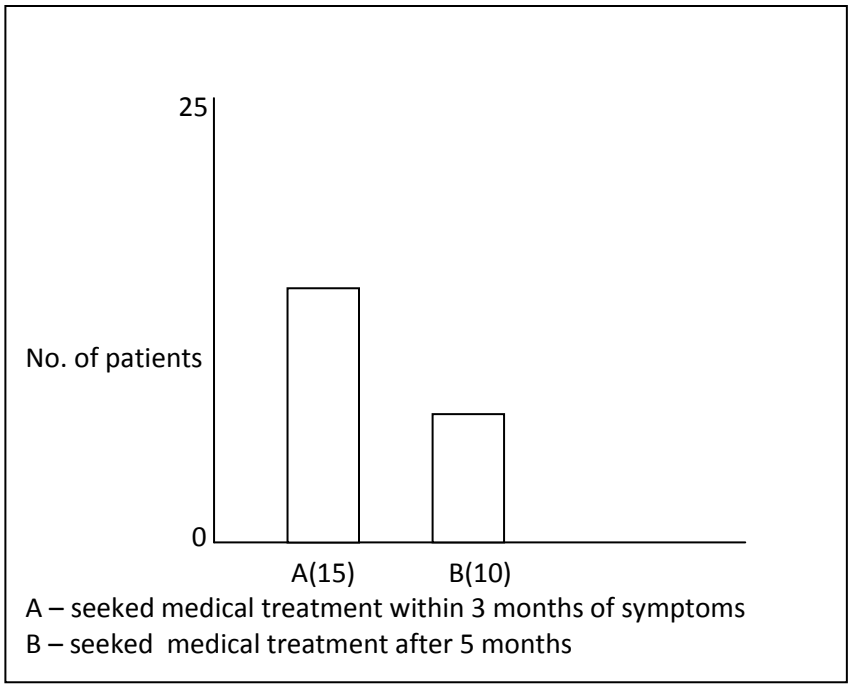
5) COMPLIANCE OF ATT



A	9/25	65%
B	5/25	20%

In our study, of the patients with past history of PT only 20% completed ATT

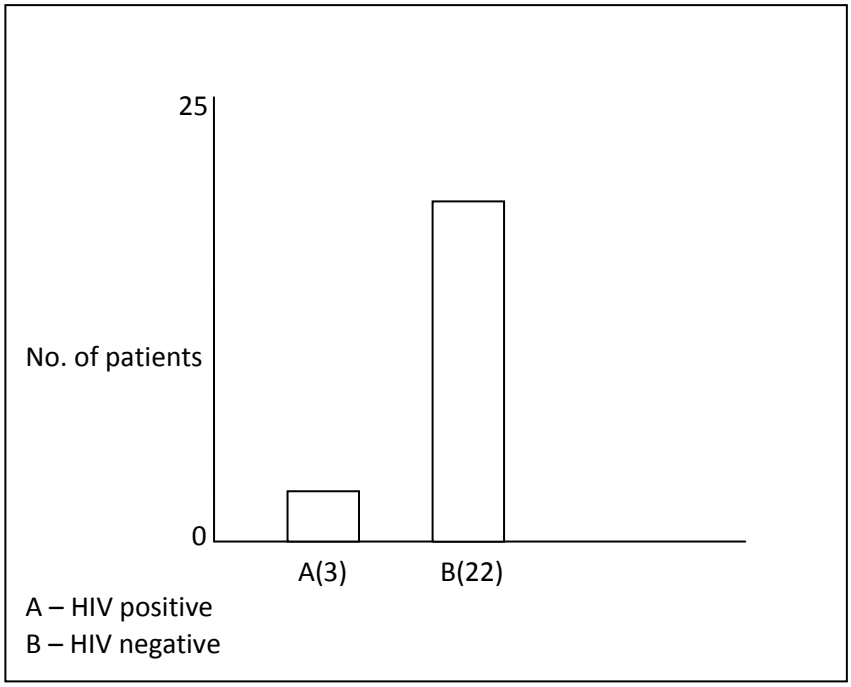
5)TIME OF REPORTING



A	15/25	60%
B	10/25	40%

60% of patients presented to hospital within three months of symptoms.

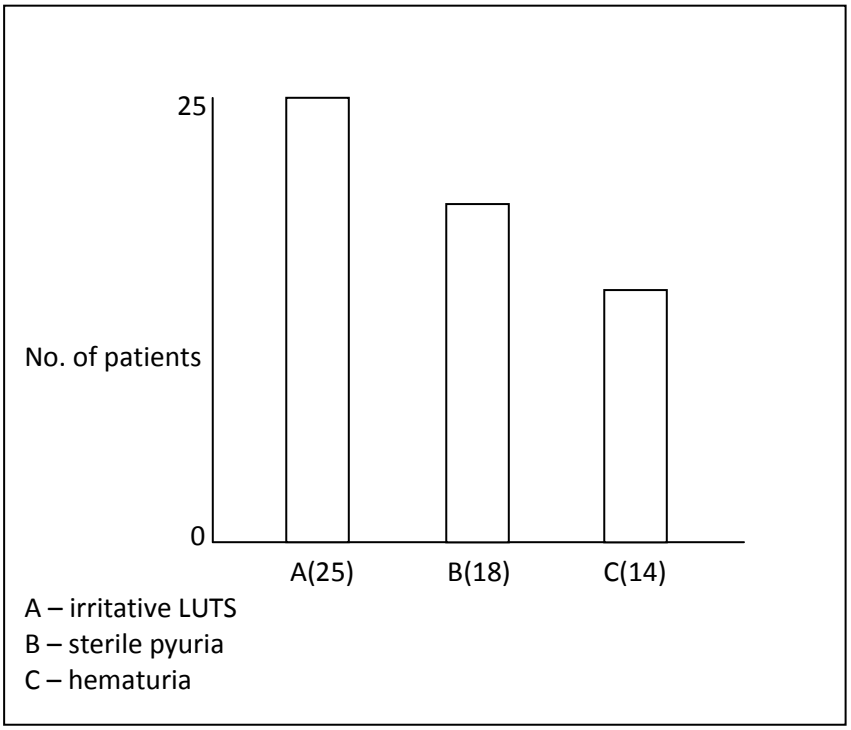
6)GUTB WITH RETRO POSITIVITY



A	3/25	12%
B	22/25	88%

12% of patients of our study sample were HIV positive

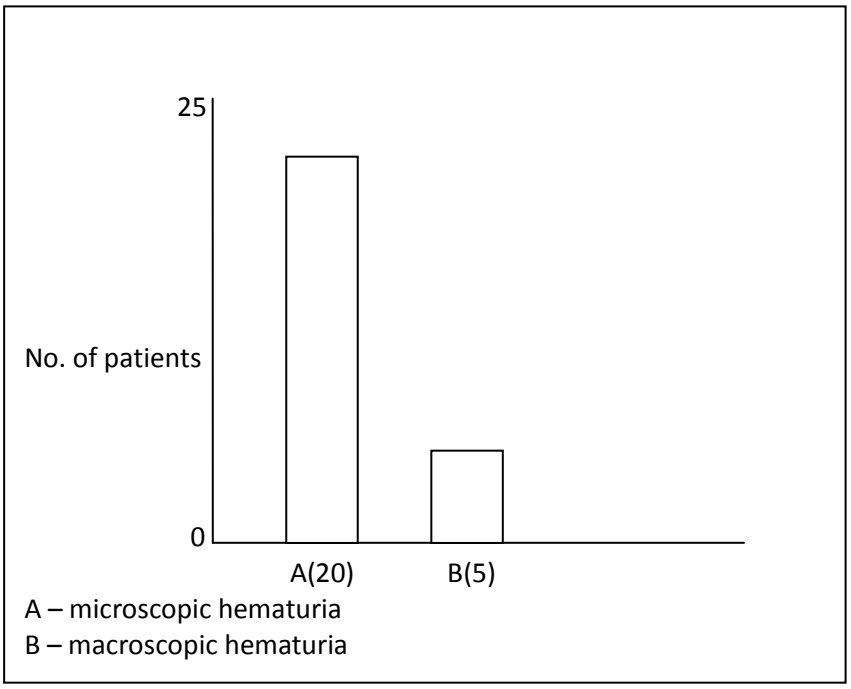
7)SYMPTOMS OF GUTB



A	25/25	100%
B	18/25	72%
C	14/25	56%

100% of patients in our study group presented with irritative LUTS. Only 56% of patients had hematuria.

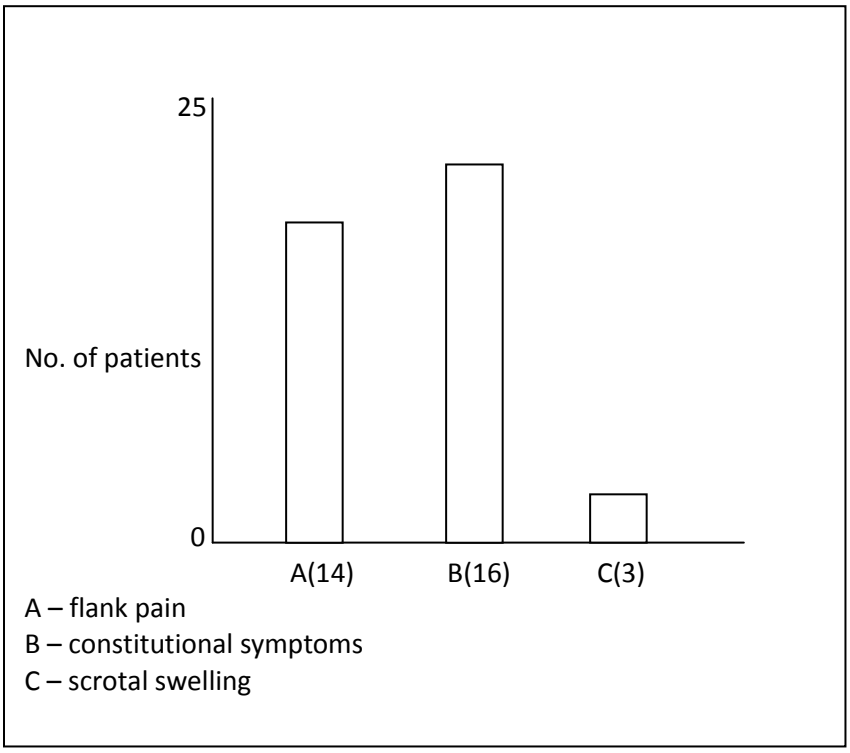
8)SYMPTOMS OF GUTB



A	20/25	80%
B	5/25	20%

80% of patients had only microscopic hematuria

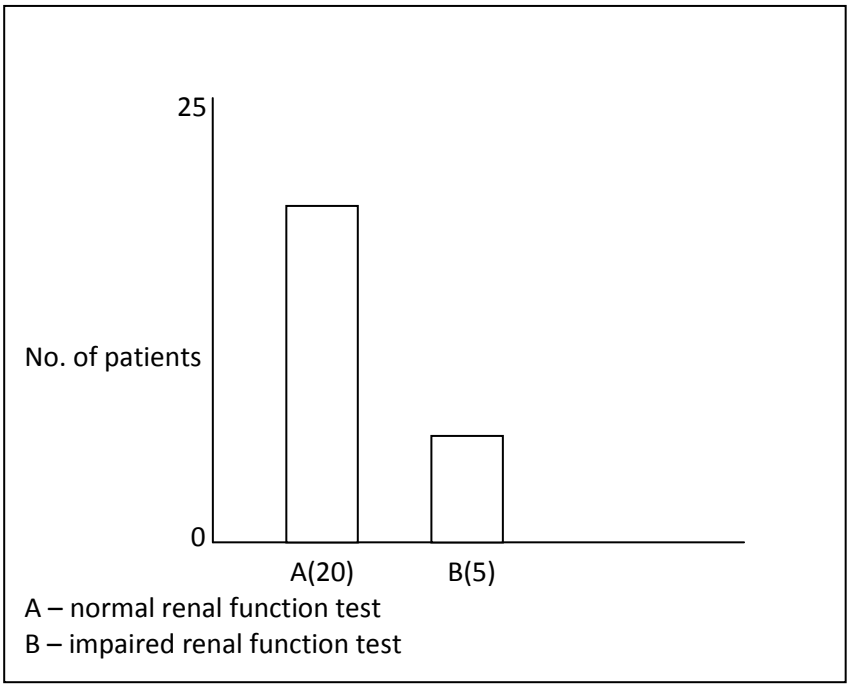
9)SYMPTOMS OF GUTB



A	14/25	56%
B	16/25	62%
C	3/25	15%

62% of patients had constitutional symptoms like low grade fever, loss of weight and appetite

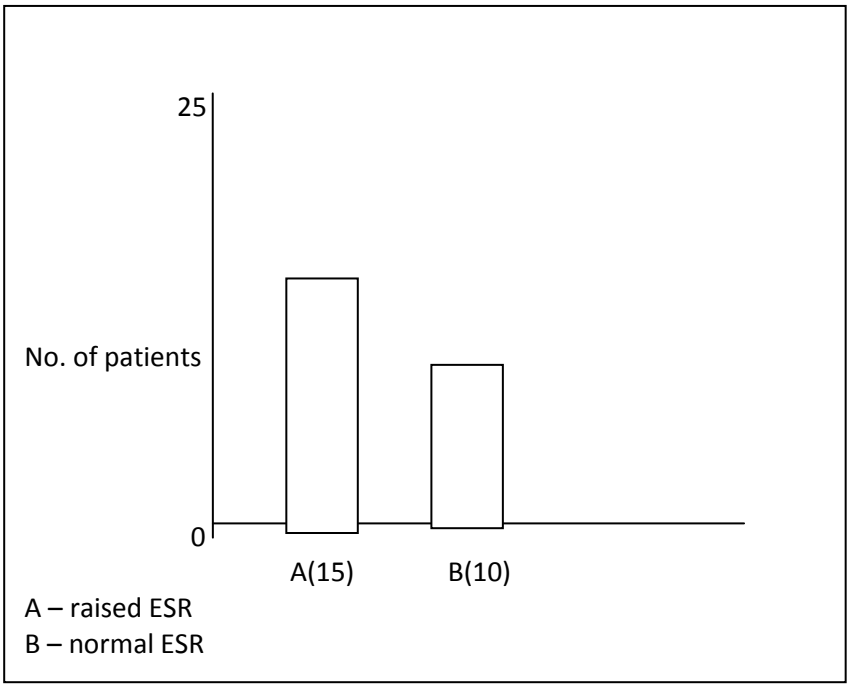
10)RFT IN GUTB



A	20/25	80%
B	5/25	20%

80% of our patients had normal renal function

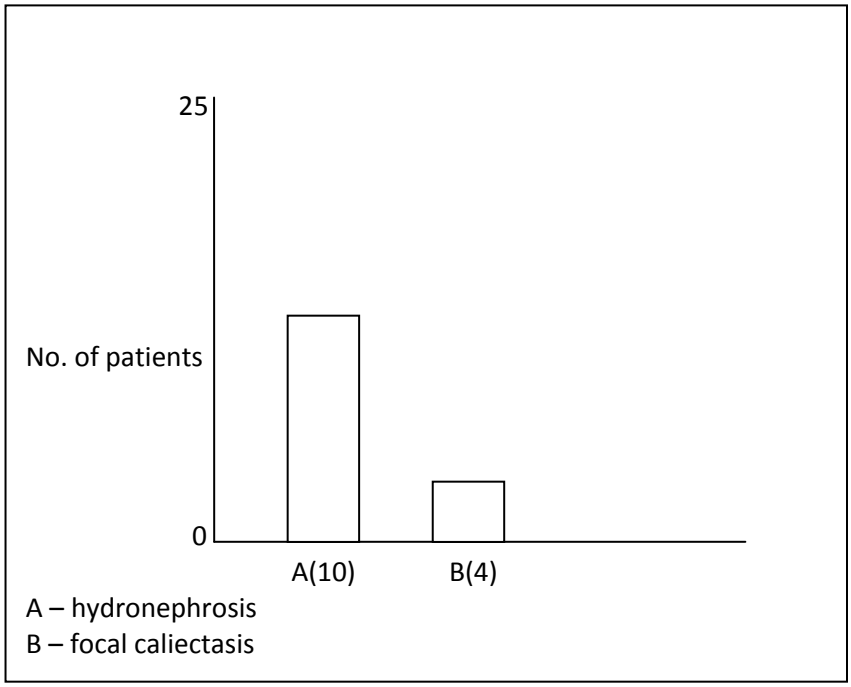
11)ESR IN GUTB



A	15/25	60%
B	10/25	20%

60% of our patients had raised ESR

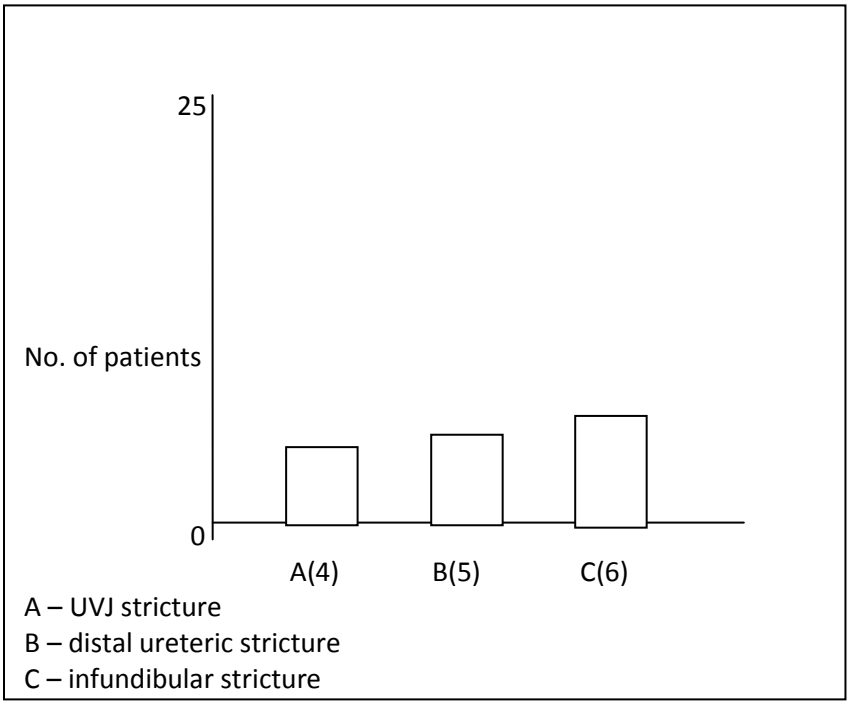
12)IVU FINDINGS



A	10/25	40%
B	4/25	8%

40% of patients had hydronephrosis while 8% of patients had focal caliectasis.

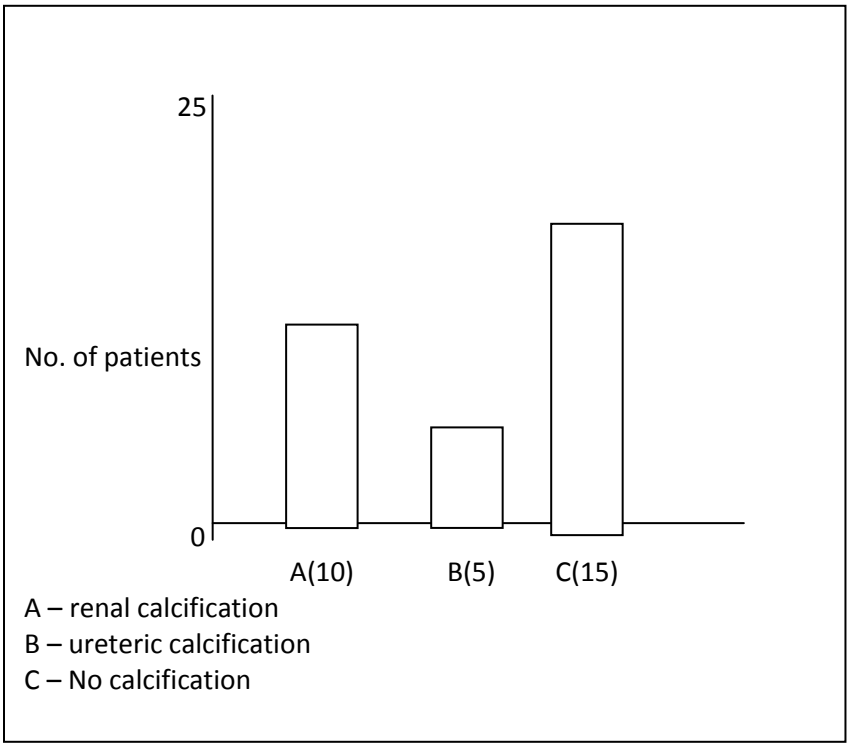
13) FINDINGS IN IVU



A	4/25	16%
B	5/25	20%
C	6/25	24%

Most of our patients had infundibular stricture followed by distal ureteric stricture

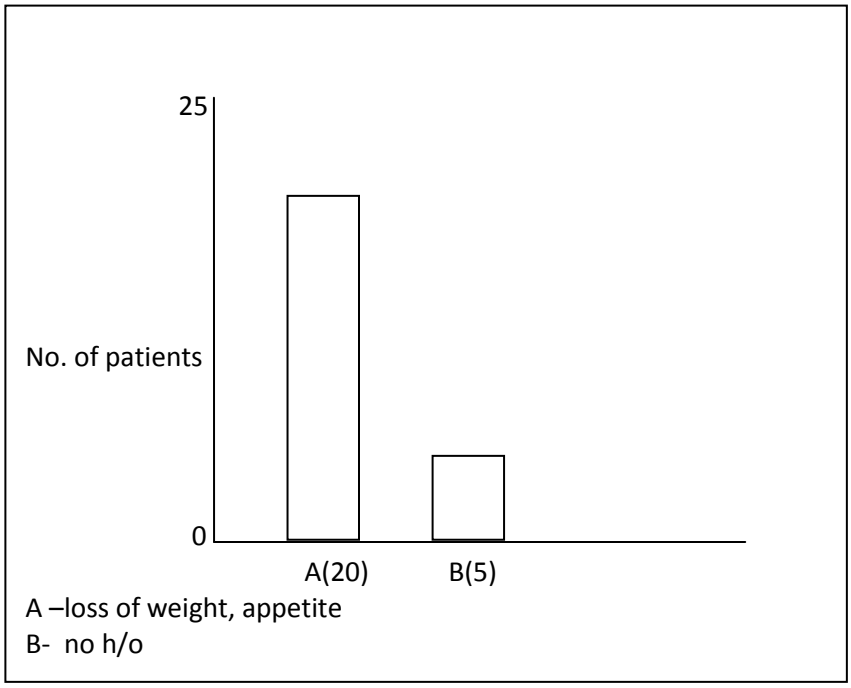
14)FINDINGS IN IVU



A	10/25	40%
B	5/25	20%
C	15/25	60%

60% of our patients did not have any calcification in IVU

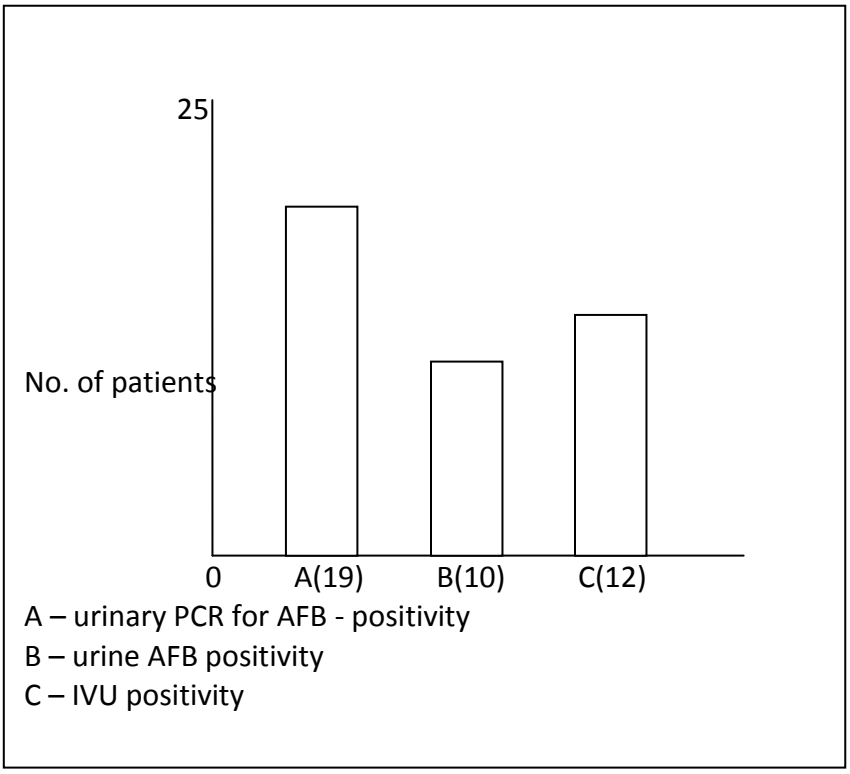
15)CONSTITUTIONAL SYMPTOMS



A	20/25	80%
B	5/25	20%

80% of our patients had loss of weight and appetite

16)POSITIVITY OF INVESTIGATION



A	19/25	76%
B	5/25	20%
C	12/25	50%

76% of our patients were diagnosed GUTB by urinary PCR method

RESULTS & ANALYSIS

RESULTS & ANALYSIS

SAMPLE SIZE : 25

Total No. of Males : 18

Females : 7

Most common age group : 30 to 40 years

: 40 to 45 years

Symptoms / Variables

Irritative LUTS – 25

Sterile pyuria – 18

Hematuria – 14

Flank pain – 14

Constituitional symptoms - 16

Scrotal swelling – 3

Sinus / fistula – nil

No. of patients subjected to following investigations

Urine AFB – 25

Urine PCR – 25

IVU – 25

Results

No. of patients diagnosed of GUTB from these investigations – 19

No. of patients with past history of PT – 12

No. of patients with active PT - nil

No. of Urine AFB positivity – 10/25

No. of Urine PCR positivity – 19/25

No. of IVU positivity – 12/25

ANALYSIS

COMPARISON BETWEEN URINE PCR AND URINE AFB

Diagnostic technique	Urine PCR		
Urine AFB	Positive	Negative	Total
Positive	10	0	10
Negative	9	6	15
Total	19	6	25

Sensitivity – 52.6%

Specificity – 100%

PPV – 100%

NPV – 66.7%

False negative % – 47.4%

False positive % – 0%

Accuracy – 64%

COMPARISON BETWEEN URINE PCR AND IVU

Diagnostic technique	Urine PCR		
IVU	Positive	Negative	Total
Positive	12	0	12
Negative	7	6	13
Total	19	6	25

Sensitivity – 63.2%

Specificity – 100%

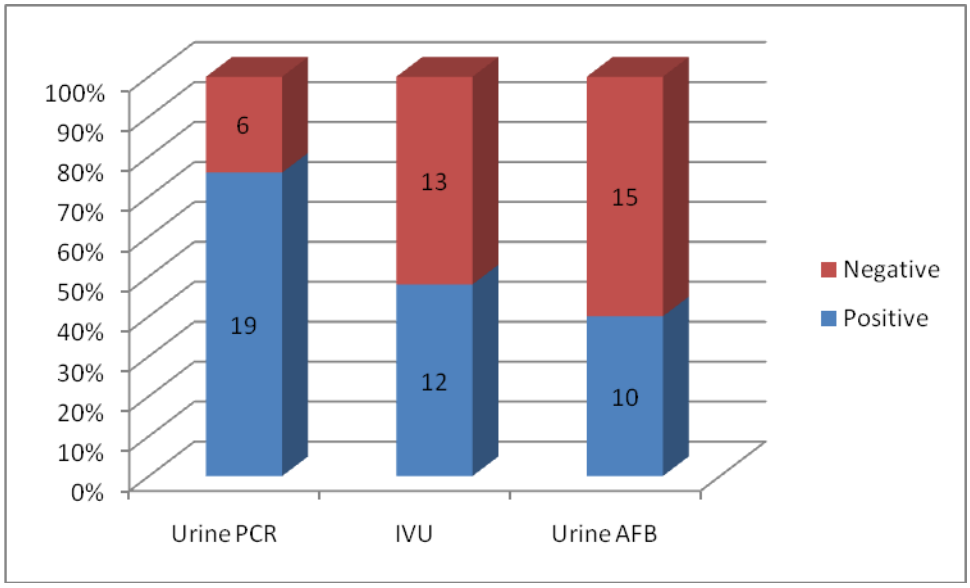
PPV – 100%

NPV – 46.2%

False negative % – 36.8%

False positive % – 0%

Accuracy – 72%


100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
6
19
13
12
15
10
Urine PCR
IVU
Urine AFB
Negative
Positive

DISCUSSION

DISCUSSION

Two important process are involved in diagnosing GUTB

1) A high index of suspicion of GUTB
2) demonstration of Tubercle bacilli in urine sample

Detection of AFB in urine is usually done by ZIEHL-NEELSON staining method. It is not as reliable as culture and sensitivity to make a diagnosis of GUTB because of cross contamination with M.Smegmatis. 3-5 consecutive early morning whole urine is a must for diagnosing by this method. If at all urine AFB should be positive the sample should contain atleast10000 bacteria per ml to give a slide positivity.

Due t1o the fact that GUTB is a pauci-bacillary condition, this method is more prone for false negative results.

Polymerase chain reaction test is based on nucleic acid replication technique. The mycobacterial DNA in urine sample is sufficient for diagnosing GUTB. The PCR detection limit of mycobacterial DNA is above 5-10 FG which equivalent to 3-5 mycobacteria.

The following PCR tests are available with excellent quality and result.

1) Roche Amlplicor MTB PCR test
2) Amplified Mycobacterium TB Direct Detection Test(AMDT)
3) Genus-specific 16SrRna PCR Test
4) Species-specific IS6110 PCR test.

Although new radiological investigations are in use extensively IVU still remains one of the preferred investigation in the diagnosis of GUTB.

The sensitivity of urine AFB varies from 30-60% based on single or multiple specimen. The sensitivity of urinary PCR ranges from 88-92%, the sensitivity of IVU varies from 82-85%.

In our study the disease is most commonly seen in males, about 76% mostly in the sexually active period of life.(20-40yrs – 80%).

The variable significant results are

About 56% of patients had past history of PT, of which only 36% had completed ATT. 60% of patients attended hospital within 3 months of symptoms. 12% of patients were positive for retro virus. 80 % of patients in our study had normal renal functions. 60% of patients had raised ESR. 72% of

patients had sterile pyuria. 100% of patients had irritative LUTS. About 56% of patients had hematuria of which 80% was microscopic hematuria. Only 56% of patients had flank pain and 15% had scrotal mass.

In IVU only 40% of patients had renal and ureteral calcification while 60% did not have any calicification.

The various findings of GUTB are also plotted in bar diagram, the most common finding being VUJ narrowing,(16%) distal ureteric stricture(20%) and infundibular narrowing.(24%)

In our study urinary PCR was compared with urine AFB and IVU findings.

In a study conducted by National Medical Centre of the Mexican Health Institute, they have concluded that the sensitivity of PCR varied between 88% to 92.2% with a specificity of 78.7%.

In our study urinary PCR was positive in 76% of patients while IVU was positive in 50% of patients and urine AFB was positive in only 20% of patients, which is comparable to a study conducted at AIIMS, Newdelhi as mentioned below.

In another study conducted by department of urology and microbiology at AIIMS, NewDelhi, the sensitivity of urinary PCR range from 70.95% to 85% whereas the sensitivity of urine AFB was about 22-40%, the sensitivity of IVU range from 70 to 80%.

COMPARING URINARY AFB WITH URINARY PCR

In our study the sensitivity of urinary PCR detecting GUTB varied between 75 to 80%, when comparing with urine AFB the sensitivity of urine AFB was found to be 52.6% and specificity of 100%.

The positive predictive (PPV) of urine AFB was 100%

The negative predictive value being 66.7%

False positivity was 0%, false negativity 47.4%

The accuracy of detecting GUTB by urine AFB method is about 64%

COMPARING IVU WITH URINARY PCR

In our study all 25 patients underwent IVU and the results were compared as follows :

50% of patients showed features of GUTB in IVU.

The sensitivity of IVU when compared with urine PCR for diagnosing GUTB is about 63.2%(±5%)

The sensitivity being 100%. The positive predicted value(PPV) of IVU is 100%. The negative predicted value (NPV) is 46.2%, the false positivity is 0%, the false negativity is about 36.8%. The accuracy of IVU in detecting GUTB was about 72%.

CONCLUSION

CONCLUSION

In developing countries like India Tuberculosis is an important public health problem, most so the detection and management of GUTB. Timely and early diagnosis will prevent late complication of GUTB like TB Pyonephrosis, non functioning kidney and thimble bladder.

Since about 8-15% of patients history of PT are prone to develop GUTB it is essential to have a rapid diagnosis. PCR is one of the best tool for avoiding delay in diagnosis and treatment since the results are available in 4-6 hrs whereas culture takes 6-8 weeks of time.

A controlled PCR can help in either excluding or confirming diagnosis of GUTB. Since GUTB is a pauci bacillary condition, PCR has a prominent role in diagnosis.

The limit of detection of MTB by urinary PCR ranges between 1 - 10 bacteria.(1FGDNA vial – 1 bacteria contains 5FGDNA)

Moreover there is no crossover reaction occurs with other mycobacteria. The false negativity in urinary PCR can be decreased by the following ways :

1) Removing PCR inhibitors
2) Concentrating sample before analysis
3) Testing multiple specimen of same patient
4) Testing quality specimen.

False positivity in PCR may be due to contamination by amplicons (MTB complex bacteria or DNA) and dead bacteria.

The drawbacks of urinary PCR is the need for experienced staff, the cost, and a small no. of samples being done in both private and Government sectors.

Our study concludes that of the three investigations we compared (URINE PCR FOR MTB, URINE FOR AFB, IVU) URINE PCR for MTB is the most sensitive indicator in diagnosing GUTB as it gives a RAPID, SENSITIVE and SPECIFIC results.

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BIBLIOGRAPHY

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ANNEXURE

ANNEXURE

AIM :

'To compare the sensitivity of Urinary Polymerase chain reaction(PCR) with intravenous urography and urine acid fast bacilli culture in a clinically suspected case of GUTB'

Materials and methods:

- **Study Group** : patients who are admitted in Kilpauk Medical College and Govt. Royapettah hospital with irritative lower urinary tract symptoms due to GUTB
- **Study Design** : prospective clinical study
- **Study Period** : 1 Year
- **Inclusion Criteria** :
    - Patients with complaints of
- irritative voiding symptoms
- sterile pyuria
- hematuria
- constitutional symptoms – low grade fever
    - loss of appetite/weight
- flank pain
- scrotal sinus / swelling

EXCLUSION CRITERIA :

OTHER CAUSES OF STERILE PYURIA,

IRRITATIVE LOWER URINARY TRACT SYMPTOMS,

HEMATURIA ARE RULED OUT .

PROFORMA

NAME : AGE : SEX :

ADDRESS ; IP.NO.

D.O.A. D.O.D

PRESENTING COMPLAINTS

H/O URGENCY

INCREASED FREQUENCY

DYSURIA

NOCTURIA

HEMATURIA

H/O. EVENING RISE OF TEMPERATURE

H/O LOSS OF WEIGHT / APPETITE

PAST HISTORY – COMORBID ILLNESS – PULMONARY TUBERCULOSIS

GENERAL EXAMINATION: PR: BP:

CARDIO VASCULAR SYSTEM

RESPIRATORY SYSTEM

PER ABDOMEN:

GENITAL EXAMINATION

SCROTAL EXAMINATION :

PER RECTAL EXAMINATION :

INVESTIGATIONS

URINE – ROUTINE EXAMINATION

FOR ACID FAST BACILLI

POLYMERASE CHAIN REACTION(PCR)

HB%: PCV%: ESR: ½ HOUR 1 HOUR

BLOOD UREA

SUGAR

SERUM CREATININE

ELECTROLYTES

ULTRASONOGRAM

CHEST XRAY

PLAIN XRAY KUB

INTRAVENOUS UROGRAM

CYSTOSCOPY

IMPRESSION

INSTITUTIONAL ETHICAL COMMITTEE
GOVT.KILPAUK MEDICAL COLLEGE,
CHENNAI-10
Ref.No.3393/ME-1/Ethics/2013 Dt:27.09.2013
CERTIFICATE OF APPROVAL

The Institutional Ethical Committee of Govt. Kilpauk Medical College, Chennai reviewed and discussed the application for approval "A Study on compare the sensitivity of urinary polymerase chain reaction (PCR) with intravenous urography and urine acid fast bacilli in a clinically suspected case of GUTB" – For Project Work Submitted by Dr.S.Sudhakaran, MCh. (Uro), PG Student, KMC, Chennai.

The Proposal is APPROVED.

The Institutional Ethical Committee expects to be informed about the progress of the study any Adverse Drug Reaction Occurring in the Course of the study any change in the protocol and patient information /informed consent and asks to be provided a copy of the final report.

GOVT. KILPAUK MEDICAL COLLEGE
25 NOV 2013
Kilpauk, Chennai-10.

25/11/13.

CHAIRMAN,
Ethical Committee
Govt.Kilpauk Medical College,
Chennai

MASTER CHART

SL.NO	PATIENT NAME	AGE	SEX	I.P.NO.	IRRITATIVE VOIDING SYMPTOMS	STERILE PYURIA	HEMATURIA	CONSTITUTIONAL SYMPTOMS	FLANK PAIN	SCROTAL SINUS/SWELLING
1	RADHA	30	F	113302						
2	ILLAYAPERUMAL	45	M	1219						
3	SURESH	17	M	2643						
4	RAMALINGAM	58	M	2900						
5	RAMASAMY	36	M	4088						
6	MANIKAM	60	M	6758						
7	RAJA	37	M	8312						
8	RAMAMOORTHY	48	M	11824						
9	NAGAMMAL	30	F	21166						
10	MEGANATHAN	32	M	21842						
11	DATCHAYANI	40	F	24926						
12	SURESH	34	M	1323						
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TURNITIN REPORT